

ECONOMIC EVALUATION OF TAILORED WEB VS. TAILORED TELEPHONE-BASED INTERVENTIONS TO INCREASE COLORECTAL CANCER SCREENING AMONG WOMEN

RUNNING TITLE: Cost-Effectiveness of CRC Screening Interventions

David R. Lairson^{1*}, Tong Han Chung¹, Danmeng Huang, Timothy E. Stump², Patrick O. Monahan^{2,4}

Shannon M. Christy^{5,6,7} Susan M. Rawl^{3,4} &

Victoria L. Champion^{3,4}

¹School of Public Health, University of Texas Health Science Center at Houston, Houston, TX

²Indiana University School of Medicine, Indianapolis, IN

³School of Nursing, Indiana University, Indianapolis, IN

⁴Indiana University Simon Cancer Center, Indianapolis, IN

⁵Division of Population Science, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL

⁶Morsani College of Medicine, University of South Florida, Tampa, FL

⁷Purdue School of Science, Indiana University-Purdue University Indianapolis, Indianapolis, IN

This is the author's manuscript of the article published in final edited form as:

Lairson, D. R., Chung, T. H., Huang, D., Stump, T. E., Monahan, P. O., Christy, S. M., Rawl, S. M., & Champion, V. L. (2020). Economic Evaluation of Tailored Web versus Tailored Telephone-Based Interventions to Increase Colorectal Cancer Screening among Women. *Cancer Prevention Research (Philadelphia, Pa.)*, 13(3), 309–316. <https://doi.org/10.1158/1940-6207.CAPR-19-0376>

David R. Lairson, PhD is Professor of Health Economics and Co-director of the Center for Health Services Research at the University of Texas Health Science Center at Houston.

Tong Han Chung, PhD, MPH is a health economist for the department of Health Transformation Initiatives at the University of Texas Health Science Center at Houston.

Danmeng Huang, MPA is a Ph.D candidate in Health Policy research at the University of Texas Health Science Center at Houston.

Timothy E. Stump, MA is a Senior Biostatistician in the Division of Biostatistics of Indiana University.

Patrick O. Monahan, PhD, is a professor in Department of Biostatistics at Indiana University School of Medicine and School of Public Health.

Shannon M. Christy, PhD, is an Assistant Member in the Department of Health Outcomes and Behavior at Moffitt Cancer Center.

Susan M. Rawl, PhD, RN, FAAHB, FAAN, is a professor at Indiana University School of Nursing.

Victoria L. Champion is the Distinguished Professor in Nursing and the Associate Director of Population Science and Community Outreach at Indiana University Simon Cancer Center.

Key Words: colorectal cancer, screening, cost-effectiveness, web-based, telephone counseling

Acknowledgements:

- This research was supported by the National Cancer Institute (5R01CA136940-02, PI: Victoria L. Champion), and was registered with the clinical trials identifier NCT03279198 <https://clinicaltrials.gov/show/NCT03279198>. The efforts of Shannon M. Christy were supported by the National Cancer Institute while she was a predoctoral fellow at Indiana University-Purdue University Indianapolis (R25CA117865; PI: V. L. Champion) and while she was postdoctoral

fellow at Moffitt Cancer Center (R25CA090314; PI: T. H. Brandon). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Danmeng Huang was supported by a Predoctoral Fellowship, University of Texas School of Public Health Cancer Education and Career Development Program – National Cancer Institute/NIH Grant R25 CA57712 and by the Institute of Public Policy.

- David R. Lairson, Tong Han Chung, and Danmeng Huang had full access to all of the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis. David R. Lairson, Tong Han Chung, Danmeng Huang, all from University of Texas Health Science Center at Houston, conducted and are responsible for the data analysis and interpretation. Victoria L. Champion and Susan M. Rawl lead the community-based trial. Timothy E. Stump and Patrick O. Monahan conducted data cleaning and multiple imputation analysis. Shannon M. Christy and all other co-authors contributed to manuscript review and writing, and approved the final manuscript.

*Corresponding Author: David R. Lairson

Address: 1200 Pressler St. Houston, TX 77030

Suite RAS-E307

Telephone: +1 (713) 500-9176, Fax: 713-500-9171

Email: David.R.Lairson@uth.tmc.edu

Conflict of Interest: No potential conflicts of interest were disclosed by the authors of this paper.

Abstract:

Screening for colorectal cancer (CRC) is cost-effective, but many U.S. women are non-adherent, and the cost-effectiveness of web-based tailored screening interventions is unknown. A randomized controlled trial, COBRA (Increasing Colorectal and Breast Cancer Screening), was the source of information for the economic evaluation.

COBRA compared screening among a Usual Care group to: 1) tailored Phone Counseling intervention, 2) tailored Web intervention, and 3) tailored Web + Phone intervention groups. A sample of 1196 women aged 50-75 who were non-adherent to CRC screening were recruited from Indiana primary care clinics during 2013-2015. Screening status was obtained through medical records at recruitment with verbal confirmation at consent, and at 6-month follow-up via medical record audit and participant self-report. A "best sample" analysis and micro-costing from the patient and provider perspectives were applied to estimate the costs and effects of the interventions. Statistical uncertainty was analyzed with non-parametric bootstrapping and net benefit regression analysis.

The per participant cost of implementing the Phone Counseling, Web-based, and Web + Phone Counseling interventions was \$277, \$314, and \$336, respectively. The incremental cost per person screened for the Phone Counseling compared to no intervention was \$995, while the additional cost of Web and the Web + Phone compared to Phone Counseling did not yield additional persons screened.

Tailored Phone Counseling significantly increased CRC screening rates compared to Usual Care.

Tailored Web interventions did not improve the screening rate compared to the lower cost Phone Counseling intervention.

Introduction:

Colorectal cancer (CRC) is the third most common cancer and cancer-related cause of death in United States (U.S.) women [1]. One in 25 U.S. women will be diagnosed with CRC in their lifetime [1]. In 2019, it is estimated that there will be 67,100 estimated new CRC cases among U.S. women and 23,380 deaths [1]. Although CRC screening is effective in reducing CRC incidence and mortality [2], is cost-effective [3], and is covered by the Affordable Care Act, screening rates among women (63.1% in 2015) remain below the Healthy People 2020 target of 70.5% (<https://www.healthypeople.gov/2020/data/disparities/summary/Chart/4054/2>).

Behavioral interventions including mailed reminders or FIT kits, financial incentives, provider-based education, telephone counseling and patient navigation have been shown to increase CRC screening [4-7]. Moreover, tailoring the intervention message on demographic and belief variables can further increase the effect [8-10]. However, whether an intervention is an efficient use of scarce healthcare resources partially depends on its cost. Depending on their complexity, type of personnel employed, and the types of costs included, the reported cost to deliver tailored CRC screening interventions ranges from \$5.48-\$45 [11-14], while other CRC screening interventions such as postcard reminders and patient navigations range widely from \$2.49-\$1,089 per participant [15-19]. The wide range of cost estimates indicate large variation in costs due to heterogeneity in the intervention designs and delivery modalities. More importantly, to better evaluate the relative efficiency of the interventions, we still need to consider their cost and yield of additional non-adherent persons screened through a function of incremental cost and effectiveness. The incremental cost-effectiveness ratios (ICER) are \$15-\$21,124 per additional person screened [11-17, 19, 20]. Among those interventions, tailored interventions have reported

ICERs from \$94-\$1,643 [11, 12, 14] depending on the intervention design, types of costs included, and the effectiveness of interventions to increase CRC screening.

A randomized controlled trial (RCT) used a full 2X2 factorial design to compare the efficacy of a tailored Web intervention, a tailored Phone Counseling intervention, and the tailored Web + Phone interventions combined versus Usual Care for promoting CRC screening among women not up-to-date with CRC screening recommendations. Compared to previously studied interventions, the ones tested in the RCT were designed to tailor intervention messages on a comprehensive set of demographic, beliefs, and stage-of-change to screen. The outcomes of the RCT showed that compared to Usual Care, the Phone and the Web + Phone interventions significantly increased CRC screening rates [21]. The current cost-effectiveness study was conducted concurrently with the efficacy trial, with the goal to inform researchers and decision makers about the economics of tailored interventions with alternative communication technologies for increasing CRC screening rates.

Materials and Methods:

Champion et al. (2018) provide details of the interventions, methods, and screening results of the trial [21]. Briefly, Indiana University and community intervention clinics' institutional review boards approved the study protocol. Enrollment was completed from 2013-2015, and included 1,196 women from two primary care health centers, identified from medical records indicating no recent stool test (e.g., fecal immunochemical test [FIT]) or colonoscopy. Participants were women aged 50 to 75 years old with internet access who did not complete a stool test in the past

15 months, a sigmoidoscopy in the last 5 years, or a colonoscopy in the last 10 years. Exclusion criteria were: 1) a personal history of CRC, colorectal polyps, or inflammatory bowel disease, and 2) any medical conditions that would prohibit CRC screening. Participants completed written consent, and were surveyed at baseline, 4 weeks, and 6 months, and received a \$20 gift card after completing each survey. Medical records documented screening status 6 months post-intervention. The study was conducted in accordance with U.S. Common Rule.

Tailored Interventions:

Tailoring was based on demographic variables (e.g., age, race), health belief variables (e.g., perceived barriers), and objective risk for developing CRC [22, 23]. An assessment of objective CRC risk based on family history of colon cancer informed messages about risk-appropriate CRC screening tests [1, 24, 25]. Women at higher than average risk received messages that encouraged colonoscopy, while women at average risk could choose to hear messages about either stool test or colonoscopy. Messages and tailoring algorithms were adapted from past tailored cancer screening interventions.

Web Intervention: The web intervention included photographs, video clips, animations, and graphics and tailored messages. Tailored messages for all potential participant responses to tailored variables were filmed and algorithms built such that the program a participant viewed was unique to their individual answers [26]. Written information was accompanied by audio narration, allowing women with low literacy to use the program.

Phone Counseling Intervention: A computer-tailored program was used to structure the Phone Counseling session. The computer interface provided the message content after the

interventionist queried a participant to gather data needed for tailoring messages. Participants in the Phone Counseling group received tailored messages similar to those provided in the Web program. Phone interventionists were trained to deliver the program during an intensive 2-day session.

Web + Phone Intervention: Women in the combined Web + Phone intervention were encouraged to complete the Web intervention prior to receiving Phone Counseling.

Usual Care: The Usual Care group did not receive an intervention. However, depending on the location where they received primary care services, they may have received a postcard reminder for cancer screenings.

Cost estimation:

Costs were estimated from the provider and participant perspectives for each intervention group and summarized by major activity, including planning and program monitoring, data management, identification and recruitment of eligible participants, intervention staff training, intervention delivery, materials, and overhead. The costs of recruitment, staff training, general management and monitoring, and materials were averaged across intervention groups. All of the interventions require these activities and applying an average cost for all groups avoided penalizing an intervention due to random factors that may have caused higher costs. The mean web-specific costs and phone specific costs were separately applied to the appropriate intervention groups. The material and personnel time cost for each project activity was determined by prospective micro-costing, where the resource use was tracked with time logs and invoices, and weighted with local unit prices, inflated to 2016 U.S. dollars by the U.S. consumer

price index – medical care component (<https://data.bls.gov/pdq/SurveyOutputServlet>). The personnel time cost, the material cost, and the overhead cost added up to total cost. Intervention development cost was estimated and published previously [27], but excluded from the cost-effectiveness analysis, as it was considered a sunk cost (i.e., the cost would not be incurred in future implementations of the intervention).

Personnel time cost:

Personnel time data were obtained from monthly electronically reported staff logs for minutes spent on program activities. The staff were regularly reminded to record their time log by the cost data collector and the project manager requested staff to complete their time log if they failed to report their time log for more than three months. Research time, including informed consent, baseline interviews (except for determining eligibility and risk level), follow-up interviews, and chart reviews were not included in the intervention cost. The personnel time cost was calculated by multiplying the minutes per activity by the adjusted salary per minute of the individual staff. The adjusted salary per minute was calculated using staff salaries, fringe benefit rates, available work time after adjusting for holidays and vacation days, and assuming an 85% productivity rate [28].

Fixed time costs were activities by staff that occurred prior to the delivery of the first interventions, including 1) planning meetings with project personnel and clinic staff for roll-out of the intervention, 2) training of phone counselors, and 3) set up and initial testing of the website for the Web and Web + Phone Interventions (hereafter referred to as website). Variable

personnel time costs included personnel time associated with each participant engaged in the intervention. Items include 1) identifying potential participants, verifying eligibility, and enrolling potential intervention participants, 2) maintenance of the website and solving participant issues with use of the site, 3) participant time on the website, 4) preparation for and call time (both connected and failed) for Phone Counseling by staff and participants. Time spent by the participants interacting on the website was automatically tracked when they logged onto the site. Time spent by staff and participants during Phone Counseling was recorded. A multiple imputation (MI) using Markov Chain Monte Carlo method was used to impute missing phone call time. The covariates considered for MI were age, race, marital status, education, employment status, and income level. Through the three MI procedures (imputation, analysis, and pooling), the average parameter estimates of the regression model were calculated using 10 imputed datasets.

Material Costs:

Material costs include office supplies, phone calls, printing, FIT kits, FIT lab fee, and postage.

Overhead costs:

Overhead costs covering space, office equipment, and utilities were estimated at 30% of the direct costs [15].

Participant Cost:

Participant time cost was calculated by multiplying the time participants spent on the interventions by the mean hourly wage rate for U.S. women; the age adjusted hourly wage rate of full-time workers for full-time employed women, the age adjusted hourly wage rate for workers paid by the hour for part-time employed women and the federal minimum wage rate for participants with no or missing employment status (<https://www.bls.gov/opub/reports/womens-earnings/2016/home.htm>).

Effect Estimation:

The screening compliance for each participant -a binary variable- was obtained from the COBRA randomized trial. The effectiveness of each intervention was the percentage of participants in each group who completed a colonoscopy or stool test 6 months post-intervention. Participants were deemed screened if either self-report or medical record data indicated completion of a stool test or colonoscopy. Considering the 18%-27% attrition rate across groups, we compared those lost-to-follow-ups to participants with complete data. We found no significant difference between them in demographic characteristics (age, race, marital status, education, employment status, and income level). Therefore, participants lost to follow-up were excluded in the primary analysis.

Cost-Effectiveness analysis:

Using Microsoft Excel 2013 and SAS version 9.4 (SAS Institute, Inc., Cary, North Carolina, USA), a cost-effectiveness analysis was conducted to identify the most efficient strategy for increasing CRC screening compliance compared to Usual Care. The incremental cost-

effectiveness ratios (ICERs) were computed by dividing the incremental cost of an intervention by the incremental effect of the intervention by sequentially comparing Usual Care to the Web group, the Web group to the Phone group, and the Phone group to the Web + Phone group. The sensitivity of the incremental cost-effectiveness ratios was assessed by computing changes in the ICER with changes in the main uncertain parameters, including the overhead rate, range between 0% and 40% and the scale of the program, range between 1,000 and 5,000 potential participants. Costs and effects were not discounted due to the relatively short duration of the time between the intervention and follow-up.

Statistical uncertainty in the cost and effect estimates was assessed with bootstrapping (1000 replicates of the cost-effectiveness ratios) and net benefit regression analysis adjusted for covariates to obtain 95% confidence intervals for the ICERS and a cost effectiveness acceptability curve showing the likelihood of an intervention being cost-effective given hypothetical willingness to pay for an additional person screened.

Results:

The majority of participants enrolled were Caucasian, overweight or obese, and had more than a high school education and an annual household income >\$30,000. The average age of participants was 58.9 years. Despite randomization, there were several significant demographic differences between groups. For example, the Web and Web + Phone groups had significantly more Black participants, while the Usual Care and Web + Phone groups had significantly more Asian participants. More individuals in the Web and Web + Phone groups reported going to

doctors three or more times last year compared to those in the other groups. There were also lower percentage of participants with depression that limited their activities in the Usual Care than in the Web + Phone group [21].

Table 1 shows the per participant cost of interventions (in U.S. dollars) by activity. The no cost Usual Care group was excluded. Identification and recruitment of eligible participants' costs comprised 53-63% of the total direct costs, while participant time cost adds less than \$3 to the average direct cost for all groups. At \$277 per participant, the Phone Counseling intervention was the least costly intervention, followed by Web (\$314) and the Web + Phone intervention (\$336).

Table 2 base case analysis shows the Phone Counseling group achieved the highest CRC screening rate among the three interventions. Therefore, the Web and Web + Phone interventions were dominated because they cost more to deliver but were not as effective as the Phone intervention. All sensitivity analyses found a similar pattern (Table 2).

We found the lowest ICER when zero overhead costs were assumed (\$597). When the simulated participant population was increased from the study size of about 300 per group to 5,000 per group, intervention cost per participant and the ICER decreased by 20%. The Phone Counseling intervention remained dominant with the cost per additional person screened declining to \$792 for the largest group.

For the Phone Counseling intervention, 95% confidence intervals around the ICER were generated with bootstrap simulation of 1000 replicates of the cost and effect differences compared to Usual Care (Supplementary Fig. S1). The cost-effectiveness acceptability curve (CEAC) comparing the Usual Care and the Phone interventions is shown in Figure 1.

The CEAC shows the probability of the Phone intervention being cost-effective given different hypothetical threshold willingness-to-pay (WTP) values that decision-makers may consider. Figure 1 shows that the Phone intervention had no chance of being cost-effective when the WTP is lower than \$700. However, the probability quickly increased and approached 100% when the WTP doubled to \$1,400. The CEACs from participant plus payer's perspectives were almost identical to the payer perspective, given that the average costs were similar from the two perspectives. We obtained the same CEAC after controlling for demographic variables that were unbalanced across groups in Net Monetary Benefit Regression analysis.

Discussion:

This study reported the cost-effectiveness analysis of three tailored interventions to increase CRC screening among non-adherent women, and found that the tailored, interactive web component was not cost-effective. Published literature on cost-effectiveness of CRC screening intervention are mixed with more studies unfavorable due to the extra cost of tailoring [11-14]. The tailored intervention which showed cost-effectiveness had other components which helped increase screening rates: educational pamphlet, FIT kit, and a stamped return envelope, and a

dedicated phone number for scheduling screening, while the only tailored information was the dates of recipients' last screening on the cover letter [14]. Therefore, evidence has suggested that in-depth tailored interventions based on demographics, determinants of health behavior, or health beliefs are not cost-effective, whether delivered in a printed form [12], or more technology involved forms such as computer-based flipchart [11] and video or an interactive web-based program [13].

The reported average costs for all interventions (\$277-\$336) in our study were higher than previously reported tailored CRC screening interventions which ranged from \$5.48-\$45 [16-19]. The previous tailored interventions had different intervention designs and level of tailoring, such as tailored messages [17, 19], reminder phone calls [17], and interactive multimedia intervention delivered on tablet or computer [16, 18]. Therefore, the heterogeneity partially accounted for the differences in costs. While the tailored and interactive intervention designs may increase the costs due to extra time spent on compiling information for tailoring the Phone Counseling and technical support for the website, higher costs were mainly due to time required to identify and recruit the eligible participants. We found that the recruitment costs accounted for 40%-49% of the total cost, which was higher than recruitment costs reported in other studies [11-13].

Although recruitment is a critical component of preventive interventions that requires resource allocation to identify eligible individuals and recruit them to research studies [29], other studies do not report recruitment costs [14, 16] probably because it was difficult to separate the cost of identifying eligible participants from research related activities (e.g., obtaining informed consent). The large proportion of recruitment costs in our interventions in fact indicates an opportunity for cost reduction and cost-effectiveness improvement by utilizing more efficient

recruitment strategy such as identifying individuals in need through electronic health records.

Targeting multiple preventable conditions will also spread the recruitment cost among multiple preventive services [15] and therefore improve the cost-effectiveness of our interventions.

Our analysis also showed that the tailored, interactive web component was more costly to manage and to provide technical support compared to the Phone Counseling. The four times higher participant time cost of receiving Web intervention versus Phone Counseling also suggested that the Web intervention took participants longer to complete, although both interventions were tailored. Additional reasons for the higher web intervention costs may be the time spent on website management due to difficulty in learning and technical issues associated with implementing a new complex interactive web program. These issues should decline as program staff and managers gain experience with the system. Participants may also have difficulty navigating the Web intervention, especially those with limited computer skills. The lack of interaction with another human being may also be the reason that the participants in the Web group were less likely to receive the intervention. These intervention delivery problems may partially explain why the Web-only group had a lower screening rate compared to the other groups.

Compared to usual care the incremental effects of the Phone Counseling and the Web + Phone interventions in the current study were higher (27.9% and 21.9%, respectively) than other tailored, non-tailored, and provider-targeted intervention programs [11-17, 19, 30]. In line with other published studies, the Phone Counseling intervention is cost-effective although it cost \$995

per additional women screened. However, there is potential for significantly reducing costs in non-research settings with accurate patient records and effective and efficient patient communication [31].

Overhead costs account for resources that serve across different departments and programs [32]. Due to uncertainty in the extent to which overhead was already accounted in the measurement of management and monitoring costs, the low estimate of overhead cost was assumed zero for the sensitivity analysis of the effect of overhead on the ICERs. This change, compared to the base case estimate of 30% overhead rate, reduced the ICERs by about 25%.

The study sample size of approximately 300 participants randomized per group may increase the average cost per participant compared to more efficient use of the fixed costs incurred in setting-up and delivering the interventions in larger “real world” settings. The fixed costs included intervention planning, personnel training, and the cost of setting up web intervention, accounting for about 30% of the total costs (Table 2). The simulated increase in cohort size from 300 to 5,000 participants decreased the cost per participant by spreading the fixed cost over more participants, and reduced the ICER for the Phone intervention by 20%. This finding suggests that our interventions can be more cost-effective when implemented among larger population. Therefore, future screening promotion program decision-makers should consider the effects of the size of the participant population on the cost parameters of the interventions.

Net benefit regression was applied to control for covariates that were marginally unbalanced across the groups including the number of doctor visits last year, the number of self-reported health problems, and having depression that limits activities, and showed similar results compared to the regression without covariates. In addition, the consistent results from bootstrapping and net benefit regression suggested that any differences in the groups did not affect the economic results.

There are limitations in the study. The trial incurred over 20% loss to follow-up at 6 months post intervention, although those lost to follow-up were not different from the rest of participants. A sensitivity analysis examined a scenario where all those lost to follow-up failed to receive screening, and found the ICER for Phone Counseling increased to \$1,161 (95 % Confidence Interval [\$897, \$1,675]) compared to the base case. Phone Counseling remained the most cost-effective intervention. The personnel time data was self-reported. Separating research costs from implementation costs is imprecise and errors may inflate the cost estimates. Our cohort size was lower than desired in a “real world” program due to research budget limitations, which increases the average fixed costs of the interventions [29]. Simulation of the effect of cohort size on the ICERs was applied to provide some insight to how costs would be reduced in a larger program. Finally, overhead cost was estimated as a percentage of direct cost due to lack of information on fully allocated costs of space, utilities, and high-level management resources. When overhead was assumed to be fully accounted in other costs, the cost per additional person screened by the Phone intervention was reduced by about 25%. Finally, given the characteristics of our study cohort, our findings may not generalize to lower income and education groups, individuals who

are uninsured or underinsured, individuals without access to healthcare, and those that may have more limited access to phone and internet.

In summary, our study found that the tailored Phone Counseling intervention was very effective in increasing the use of any CRC screening among non-compliant women, although the cost per additional person screened was higher than found in some previous research. Cost-effectiveness can be improved by identifying potential cost reduction opportunities such as a more efficient approach to participant recruitment and coverage of a larger target population in a real world setting. Future research is needed to identify more efficient ways to identify and recruit the target population and deliver behavioral screening interventions.

Decision makers need to consider the resources available to adapt and implement the Phone Counseling intervention [33]. The feasibility of interventions depend on the resources available, including space, staff, and time for training and intervention delivery. Decision makers should consider the high cost of identifying and engaging the non-adherent population. Outreach and active engagement can be costly depending on the accuracy and efficiency of the clinic information system. In reach directed to patients who routinely visit the clinic would incur less recruitment cost. Scaled to a larger target population, the fixed costs spread over more people, potentially reducing the average cost as demonstrated in our simulation results.

References

1. Society, A.C., *Cancer Facts & Figures 2019*. 2019, Atlanta: American Cancer Society.
2. Jemal, A., et al., *Cancer statistics, 2008*. CA: a cancer journal for clinicians, 2008. **58**(2): p. 71-96.
3. Van Hees, F., et al., *Personalizing colonoscopy screening for elderly individuals based on screening history, cancer risk, and comorbidity status could increase cost effectiveness*. Gastroenterology, 2015. **149**(6): p. 1425-1437.
4. Enard, K., et al., *Patient navigation to increase colorectal cancer screening among Latino Medicare enrollees: a randomized controlled trial*. Cancer Causes & Control, 2015. **26**(9): p. 1351-1359.
5. Green, B.B., et al., *An automated intervention with stepped increases in support to increase uptake of colorectal cancer screening: a randomized trial*. Annals of internal medicine, 2013. **158**(5 0 1): p. 301.
6. Gupta, S., et al., *Comparative effectiveness of fecal immunochemical test outreach, colonoscopy outreach, and usual care for boosting colorectal cancer screening among the underserved: a randomized clinical trial*. JAMA internal medicine, 2013. **173**(18): p. 1725-1732.
7. Ritvo, P.G., et al., *Personal navigation increases colorectal cancer screening uptake*. Cancer Epidemiology and Prevention Biomarkers, 2015. **24**(3): p. 506-511.
8. Ko, L.K., et al., *Information processes mediate the effect of a health communication intervention on fruit and vegetable consumption*. Journal of health communication, 2011. **16**(3): p. 282-299.
9. Lustria, M.L.A., et al., *A model of tailoring effects: a randomized controlled trial examining the mechanisms of tailoring in a web-based STD screening intervention*. Health Psychology, 2016. **35**(11): p. 1214.
10. Zhao, X. and E. Peterson, *Effects of temporal framing on response to antismoking messages: the mediating role of perceived relevance*. Journal of health communication, 2017. **22**(1): p. 37-44.
11. Lairson, D., et al., *Cost effectiveness of lay health worker delivered interventions to promote colorectal cancer screening: A randomized trial*. Journal of Healthcare Communications, 2016. **1**(1): p. 7.
12. Lairson, D.R., et al., *Cost - effectiveness of targeted and tailored interventions on colorectal cancer screening use*. Cancer, 2008. **112**(4): p. 779-788.
13. Misra, S., et al., *Cost effectiveness of interventions to promote screening for colorectal cancer: a randomized trial*. Journal of Preventive Medicine and Public Health, 2011. **44**(3): p. 101.
14. Sequist, T.D., C. Franz, and J.Z. Ayanian, *Cost-effectiveness of patient mailings to promote colorectal cancer screening*. Medical care, 2010. **48**(6): p. 553.
15. Chirikos, T.N., et al., *Cost-effectiveness of an intervention to increase cancer screening in primary care settings*. Preventive medicine, 2004. **39**(2): p. 230-238.
16. Lee, J.K., et al., *Cost-effectiveness of a mailed educational reminder to increase colorectal cancer screening*. BMC gastroenterology, 2011. **11**(1): p. 93.
17. Meenan, R.T., et al., *A cost-effectiveness analysis of a colorectal cancer screening program in safety net clinics*. Preventive medicine, 2019. **120**: p. 119-125.
18. Rice, K., et al., *Cost - effectiveness of a patient navigation intervention to increase colonoscopy screening among low - income adults in New Hampshire*. Cancer, 2019. **125**(4): p. 601-609.
19. Shankaran, V., et al., *Costs and cost-effectiveness of a low-intensity patient-directed intervention to promote colorectal cancer screening*. Journal of clinical oncology, 2007. **25**(33): p. 5248-5253.
20. Elkin, E.B., et al., *The economic impact of a patient navigator program to increase screening colonoscopy*. Cancer, 2012. **118**(23): p. 5982-5988.

21. Champion, V.L., et al., *A Randomized Trial to Compare a Tailored Web-Based Intervention and Tailored Phone Counseling to Usual Care for Increasing Colorectal Cancer Screening*. Cancer Epidemiology and Prevention Biomarkers, 2018. **27**(12): p. 1433-1441.
22. Beeker, C., et al., *Colorectal cancer screening in older men and women: qualitative research findings and implications for intervention*. Journal of community health, 2000. **25**(3): p. 263-278.
23. Myers, R.E., et al., *Adherence to colorectal cancer screening in an HMO population*. Preventive medicine, 1990. **19**(5): p. 502-514.
24. Hesse, B.W., et al., *Meeting the healthy people 2020 goals: using the Health Information National Trends Survey to monitor progress on health communication objectives*. Journal of health communication, 2014. **19**(12): p. 1497-1509.
25. Levin, B., et al., *Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi - Society Task Force on Colorectal Cancer, and the American College of Radiology*. CA: a cancer journal for clinicians, 2008. **58**(3): p. 130-160.
26. Champion, V.L., et al., *Randomized trial of DVD, telephone, and usual care for increasing mammography adherence*. Journal of health psychology, 2016. **21**(6): p. 916-926.
27. Lairson, D.R., et al., *Estimating development cost of an interactive website based cancer screening promotion program*. Evaluation and program planning, 2015. **50**: p. 56-62.
28. Andersen, M.R., et al., *Analysis of the cost-effectiveness of mammography promotion by volunteers in rural communities*. Health education & behavior, 2002. **29**(6): p. 755-770.
29. Ritzwoller, D.P., et al., *Costing behavioral interventions: a practical guide to enhance translation*. Annals of Behavioral Medicine, 2009. **37**(2): p. 218-227.
30. Shankaran, V., et al., *Costs and Cost Effectiveness of a Health Care Provider-Directed Intervention to Promote Colorectal Cancer Screening*. Journal of Clinical Oncology, 2009. **27**(32): p. 5370.
31. Lynch, F.L., et al., *Cost-effectiveness of a tailored intervention to increase screening in HMO women overdue for Pap test and mammography services*. Preventive medicine, 2004. **38**(4): p. 403-411.
32. Drummond, M.F., et al., *Methods for the economic evaluation of health care programmes*. 2015: Oxford university press.
33. Canter, A.S., L.Z. Paige, and S. Shaw, *Helping Children at Home and School III*. Handouts for Families and Educators: NASP (CD), 2010.

Tables:

Table 1. Cost of the Interventions per Participant

Activity			Phone US \$	Web US \$	Web + Phone US \$
Personnel Cost	Identification & Recruitment of Eligible Participants	Planning & Monitoring	54.80	54.80	54.80
		Data Management	13.79	13.79	13.79
		Screening Eligibility	66.38	66.38	66.38
	Staff Training		12.69	12.69	12.69
	Intervention	General Management & Monitoring	4.50	4.50	4.50
		Phone Intervention	16.77	----	16.35
		Web Intervention	----	43.97	43.97
Material Cost	FIT Kit		1.41	1.41	1.41
	Other Materials		42.70	42.70	42.70
Total Direct Cost			213.04	240.24	256.59
Overhead Cost			63.91	72.07	76.98
Participant Cost			0.52	2.08	2.66
Total Cost			277.47	314.39	336.22

^a See Supplementary Table S1 for more details on the costs.

Table 2. Base Case ICERs and Sensitivity Analysis of the ICERs

Variable	Group	Average Cost per Participant (US \$)	Incremental Cost per Participant (US \$)	Percentage of Participants Screened (%)	Incremental Effect (%)	ICER (US \$)	95% Confidence Interval (US \$)
Best Sample Effects Estimation (Base Case)							
Best Sample (Base Case)	Usual Care	0.00	-	24.58	-		
	Phone	277.47	277.47	52.48	27.90	994.52	(774.29, 1502.10)
	Web	314.39	36.92	22.73	-29.75	dominated	
	Web + Phone	336.22	21.83	44.39	21.66	dominated	-
Payer Plus Participant Perspective for Best Sample							
Payer Plus Participant Perspective (Base Case)	Usual Care	0.00	-	24.58	-		
	Phone	277.47	277.47	52.48	27.90	994.52	(774.29, 1502.10)
	Web	314.39	36.92	22.73	-29.75	dominated	
	Web + Phone	336.22	21.83	44.39	21.66	dominated	-
Payer's Perspective	Usual Care	0.00	-	24.58	-		
	Phone	276.95	276.95	52.48	27.90	992.65	(773.24, 1499.78)
	Web	312.31	35.36	22.73	-29.75	dominated	
	Web + Phone	333.56	21.25	44.39	21.66	dominated	-

Overhead Rate							
0 (No Overhead)	Usual Care	0.00	-	24.58	-		
	Phone	213.56	213.56	52.48	27.90	765.45	(596.74, 1155.72)
	Web	242.32	28.76	22.73	-29.75	dominated	
	Web + Phone	259.25	16.93	44.39	21.66	dominated	-
30% (Based Case)	Usual Care	0.00	-	24.58	-		
	Phone	277.47	277.47	52.48	27.90	994.52	(774.29, 1502.10)
	Web	314.39	36.92	22.73	-29.75	dominated	
	Web + Phone	336.22	21.83	44.39	21.66	dominated	-
35%	Usual Care		-	24.58	-		
	Phone	288.12	288.12	52.48	27.90	1032.70	(805.10, 1573.12)
	Web	326.40	38.28	22.73	-29.75	dominated	
	Web + Phone	349.05	22.65	44.39	21.66	dominated	-
40%	Usual Care		-	24.58	-		
	Phone	298.78	298.78	52.48	27.90	1070.88	(834.87, 1616.95)
	Web	338.42	39.64	22.73	-29.75	dominated	
	Web + Phone	361.88	23.47	44.39	21.66	dominated	-

Cohort Size							
Actual Number (Base Case)	Usual Care	0.00	-	24.58	-		
	Phone	277.47	277.47	52.48	27.90	994.52	(774.29, 1502.10)
	Web	314.39	36.92	22.73	-29.75	dominated	
	Web + Phone	336.22	21.83	44.39	21.66	dominated	-
1000/Group	Usual Care	0.00	-	24.58	-		
	Phone	237.00	237.00	52.48	27.90	849.45	(662.20, 1282.56)
	Web	241.90	4.91	22.73	-29.75	dominated	
	Web + Phone	257.71	15.80	44.39	21.66	dominated	-
5000/Group	Usual Care	0.00	-	24.58	-		
	Phone	221.01	221.01	52.48	27.90	792.17	(617.55, 1196.07)
	Web	217.08	-3.93	22.73	-29.75	dominated	
	Web + Phone	233.79	16.70	44.39	21.66	dominated	-

Figure Legends:

Figure 1. Cost-Effectiveness Acceptability Curve of the Phone Intervention. The figure shows the probability of Phone counseling being cost-effective compared to Usual Care associated with different willingness-to-pay thresholds, from the perspectives of payer's and payer plus participant's. The Cost-Effectiveness Acceptability Curve was generated with bootstrap simulation of 1000 replicates of the cost and effect differences comparing Phone counseling to Usual Care.

Figure 1. Cost-Effectiveness Acceptability Curve of the Phone Intervention.

